

REMARKS

Applicant hereby requests further consideration of the application in view of the amendments above and the comments that follow. Claims 1-24 are pending in the application but stand rejected as will be discussed below.

I. The obviousness rejections based on U.S. Patent No. 5,833,608 to Acker ("Acker") in view of U.S. Patent No. 5,433,717 to Rubinsky et al. ("Rubinsky").

The Action states that Claims 1-6, 12, 14-15 and 20 are obvious over Acker in view of Rubinsky. The Examiner asserts that Acker teaches the use of a probe with an MR imaging antenna and an electrical energy application element (citing col. 9, lines 44-67) and generating a composite image using images from the surface coil and the antenna (citing col. 14, lines 6-53). Applicant respectfully disagrees.

Acker describes a probe 50 as an elongated flexible shaft and states that the probe may include "known electrical, optical or electro-optical devices for providing a local image of the tissues surrounding the distal end 56 such as video cameras and fiber-optic bundles" (col. 9, lines 58-61) (emphasis added). Clearly, this passage of Acker fails to teach or suggest a probe with an MR antenna on a distal end thereof. Also, even if this broad general statement in Acker could be interpreted to somehow include an MR antenna, there is no enabling teaching as how to configure the probe for this function, *e.g.*, no circuitry to operate the electrodes with the antenna to receive the local magnetic resonance signals (after transmit) nor how to filter RF interference and the like.

However, the Action also alleges that Acker teaches a combination imaging and therapeutic probe (citing to col. 7, lines 29-31 and col. 9, lines 44-67) and acquiring MRI images from the antenna of the combination probe, citing col. 9, lines 44-67. Again, this passage teaches images obtained from fiber-optic bundles or video cameras. Clearly, Acker does not teach a probe with an internal MRI imaging antenna, so it does not teach obtaining MRI images from that internal antenna.

Applicant respectfully reiterates that Acker does not describe an MRI system nor any

element of an MRI system other than a pre-existing image upon which data obtained by Acker's proposed system is overlaid. Indeed, none of the figures nor the text of Acker describe a functional MRI system that could produce MR images. Referring for example, to Fig. 1, the apparatus has no large magnet for producing an intense substantially uniform magnetic field "Bo" or "Bz", as taught for example in U.S. Patent No. 4,689,563, and in standard MR text books. Every one of the coil sets shown in Fig 1, produces a gradient magnetic field, as shown in Figs 3-5 of Acker. Therefore the net magnetic field at the center ($X=0$, $Y=0$, $Z=0$) of the head is zero. This is absolutely not the case in MRI, wherein a field of zero can produce no MRI signal and hence no images.

Applicant also submits that the gradient magnetic field coils that are depicted in Acker cannot be used for MRI, because they are in the incorrect orientation. In MRI, each of the imaging gradients is a gradient that is applied only in the direction of the main static field Bo or Bz, which is conventionally taken as in the Z-direction denoted by unit vector \mathbf{k} or \mathbf{z}^{\wedge} ("z-hat"). The MRI gradients are thus dBz/dx , dBz/dy , and dBz/dz : all in the direction of the z-component of the field. Therefore, even setting aside the fact that Acker has NO Bo, if Acker did, the noted gradient coils could not be used for MRI because they are not in a single field direction, but are in all 3 directions, dBx/dx , DBy/dy , dbz/dz . Therefore they cannot be used for spatially encoding an MRI signal. Finally, Acker has no radio frequency RF transmitter or receiver again meaning that the system of Acker is not used for MRI.

Applicant agrees that Acker mentions MRI (col. 11, lines 3-25), but does so only in the context of including a fiducial marker fabricated of "material that is detectable in a patient imaging technique such as X-ray...MRI... or other common imaging modalities" (col. 11, lines 15-19). In summary the Acker system is not an MRI system, cannot be used for MRI, and cannot produce MR images.

Applicant also disagrees with the Action's allegation that Ackers describes "acquiring a (plurality of) second magnetic resonance image(s) from a surface coil..." (citing to col. 8, lines 44-60; col. 11, lines 3-25) to produce a composite image (col. 14, lines 6-53). However, as noted in detail above, Acker does not describe an MRI acquisition system. Specifically, Acker does not describe acquiring second MRI images from a surface coil at the noted

passages. Acker, at col. 11, lines 3-25 mentions MRI only in the context of his invention including a fiducial marker fabricated of "material that is detectable in a patient imaging technique such as X-ray...MRI... or other common imaging modalities" (col. 11, lines 15-19). This is clearly a general reference to imaging modalities.

The text at col. 8 describes Helmholtz coils. However, contrary to the Action's assertion otherwise (p. 3), the **Helmholtz coils of Acker shown in Fig. 1 are not a conventional type of MRI RF coil**". This is incorrect as explained in 3.0 above. Helmholtz coils are conventionally NOT used for MRI, especially not RF. In particular, Acker's coils (34, 36 etc) are used to produce a gradient field (see Figs 3-5 of Acker) in the 3 Cartesian directions. The gradient coils used in MRI are produced only in the Z-direction, the direction of the main magnetic field B_0 , which Acker does not have. Even if Acker's coils were somehow used for gradients in MRI, this would then not have any MRI RF coils for MRI, nor any coils to produce the main magnetic field B_0 . If Acker's coils were used for MRI RF, then there are no coils to produce the gradient magnet fields for MRI, nor any coils to produce the main magnetic field B_0 . Either way Acker is several sets of coils short of what is needed for MRI. Furthermore, Acker's Helmholtz coils cannot be used for MRI at the crossing point ($X=0, Y=0, Z=0$) because the excitation field and sensitivity is zero there, at least one set of the coils cannot be used for MRI because the MRI RF field must be orthogonal to B_0 (which again does not exist in Acker). The Helmholtz coils proposed by Ackers are also highly undesirable for MRI because of the nonuniformity of their fields. Ackers probe in Fig 10 has temperature sensors (col. 24, lines 36-57) and "field sensing elements in the form of semiconductor chips" (col. 23, lines 40-45). Clearly, this fails to teach or suggest an MRI RF probe.

In summary, Applicant respectfully submits that it cannot be obvious to use any coils of Acker for MRI because Acker does not describe apparatus for performing MRI, and the proposed apparatus could not perform MRI even by accident as it runs counter to the theory, teaching and practice of MRI, and the coils of Acker produce the wrong kinds of fields (spatially, and frequency) for MRI.

Thus, it is impossible to produce a single MR image from the system proposed by

Acker. It is therefore impossible to produce two MR images, much less a composite MRI image.

The Action concedes that Ackers *does not teach* an RF coil as part of the probe but states that Rubinsky teaches that it is beneficial to have RF coils (such as Helmholtz coils) mounted on the surgical probe -- citing col. 14, line 50 to col. 15, line 12. The Action then concludes that it would have been obvious to incorporate the teachings of Rubinsky in order to "improve resolution of the RF coil images."

Rubinsky is directed to a cryosurgical device. Notably, at the cited text, Rubinsky states that the "surface probe 500" has an integrated RF coil (citing to Figure 4A). Rubinsky discusses spectroscopy coils 555a and 555b (for detecting ^{13}C , ^{23}Na , and ^{31}P (col. 15, line 4)) having a diameter of .6 inches (about 15 mm) and a width of .1 inch and a single turn (surface) proton coil 535 with an outer diameter of 2.8 inches (col. 15, lines 54-57) that is mounted on the outside the body 510 (col. 15, line 55). These spectroscopic coils are not imaging coils and their sizes are not appropriate for (deep) brain surgeries or other size-sensitive surgical locations in the body. Thus, Rubinsky even combined with Acker in the manner alleged would not yield the combination MRI-compatible intra-brain probes and/or methods of using same as recited in Claims 1-24.

Further, the principle of operation of Ackers coils has the sample is in the middle with the sensitive null spot at the center. If these were taken and miniaturized and put on the Rubinski cryoprobe, they wouldn't see anything of the sample, because the center of Rubinski's probe is occupied by the cryoprobe. Because the field sensitivity of Acker's coils is inappropriate for MRI (which is sensitive only to fields transverse to B_0) Acker's coils would NOT "improve resolution of the RF coil images" of Rubinski, as the Action alleges.

Applicant also respectfully submits that, even combined, Acker and Rubinsky fail to teach or suggest imaging with data from an internal MRI antenna and delivering stimulation and/or ablation signals and/or sensing electrophysiologic signals using the probe during an MRI guided interventional procedure.

Furthermore, these references do not provide enabling disclosure on how to achieve the claimed MRI intra-brain device. For example, neither Acker nor Rubinsky teach or

suggest an RF attenuation feature (Claim 15, 20, 25) or using the probe to acquire electrical signals of sensitive local tissue (*e.g.*, brain or heart) when a patient is in a high magnetic field and exposed to RF signals, such as those associated with an MRI scanner, in a manner that inhibits RF-induced electrical interference or noise (Claims 16, 20, 25 and 26).

Conventional wisdom at the time of the invention taught away from using probes or catheters with electrodes during MR imaging (*e.g.*, MRI-guided interventional procedures), particularly in sensitive regions of the body such as the heart and brain, due to the recognized dangers of undue RF heating associated with using leads, particularly those with electrodes, in an MRI Scanner or during an MRI-guided interventional procedure. *See, e.g.*, Rezai et al., *Neurostimulators: potential for excessive heating of deep brain stimulation electrodes during magnetic resonance imaging*, J Magn Reson Imaging 2001;14(4):488-489; and Chou et al., *RF heating of implanted spinal fusion stimulator during magnetic resonance imaging*, IEEE Trans Biomed Eng 1997;44(5):367-373.

The totality of the prior art must be considered, and proceeding contrary to accepted wisdom in the art is evidence of nonobviousness. *In re Hedges*, 783 F.2d 1038, 228 USPQ 685 (Fed. Cir. 1986) (Applicant's claimed process for sulfonating diphenyl sulfone at a temperature above 127°C was contrary to accepted wisdom because the prior art as a whole suggested using lower temperatures for optimum results as evidenced by charring, decomposition, or reduced yields at higher temperatures.).

Furthermore, "[k]nown disadvantages in old devices which would naturally discourage search for new inventions may be taken into account in determining obviousness." *United States v. Adams*, 383 U.S. 39, 52, 148 USPQ 479, 484 (1966).

See, MPEP 2145(X)(D)(3).

As noted above, studies employing MR Scanners have shown that, without adequate RF filters, electronics attached to the probe/catheter can malfunction during imaging. As also noted in the pending application (*see, e.g.*, Figure 5), without adequate filters, when detecting local electrophysiological signals, such as the ECG, the signal can be obscured by noise when not adequately filtered. Thus, Applicant respectfully submits that the claims are non-obvious over the cited prior art and that one of skill in the art would not have combined the references

in the manner alleged absent the teachings of the present invention. Independent claims 1, 15 and 20 are restated below for ease of reference.

1. A method of performing brain therapy, comprising:
 placing a subject in a main magnetic field of an MRI scanner during an MRI guided therapy;
 introducing into the subject's brain a combination imaging and therapeutic probe, the probe including a magnetic resonance imaging antenna and an electrical energy application element;
 acquiring a first magnetic resonance image from the antenna of the combination probe;
 acquiring a second magnetic resonance image from a surface coil;
 combining the first and second magnetic resonance images to produce a composite image;
 positioning the combination probe within the brain with guidance from at least one of the images; and
 delivering electrical energy to the brain from the electrical energy application element of the combination probe thus positioned.

15. A system for performing brain therapy, comprising:
 a magnetic resonance machine having a surface coil and means for generating a main magnetic field;
 a combination imaging and therapeutic probe, the probe including a magnetic resonance imaging antenna and an electrical energy application element;
 means for acquiring a first magnetic resonance image from the antenna of the combination probe when the antenna is inside the brain;
 means for acquiring a second magnetic resonance image from the surface coil;
 means for combining the first and second magnetic resonance images to produce a composite image;
 means for positioning the combination probe within the brain with guidance from at least one of the images; and
 means for delivering electrical energy to the brain from the electrical energy application element of the combination probe thus positioned.

20. A system for performing brain therapy using an MRI scanner, comprising:

a combination imaging and therapeutic probe, the probe including a magnetic resonance imaging antenna and an electrical energy application element on a distal end portion of the probe, the magnetic resonance imaging antenna configured to receive MR signal from local tissue *in vivo* when in position inside a subject;

means for acquiring a magnetic resonance image from the antenna of the combination probe;

means for positioning the combination probe within the brain with guidance at least in part from the image;

means for delivering electrical energy to the brain from the electrical energy application element of the combination probe thus positioned; and

an RF attenuation filter circuit in communication with the means for delivering electrical energy for selectively attenuating an RF signal in the probe generated by the MR scanner.

Applicant submits that Claims 1, 15 and 20 are patentable for at least the emphasized features and request that these rejections be withdrawn. Applicant also respectfully submits that the dependent claims recite independently patentable subject matter.

II. The obviousness rejections based on Acker and Rubinsky and further in view of U.S. Patent No. 6,045,532 to Eggers ("Eggers").

The Action states that Claims 7-11, 16-19 and 21-24 are obvious over the two above-noted references, in further view of Eggers. However, Eggers fails to remedy the deficiencies of Acker and Rubinsky, Eggers fails to teach or suggest, *inter alia*, the use of an internal MR imaging antenna. Further, Eggers is limited to energy delivery to treat aneurisms, and does not include diagnostic electrodes.

The Action concedes that Acker and Rubinsky do not disclose a diagnostic electrode, application of RF ablative current, or filtering the RF signal. Nonetheless, the Action alleges that Eggers teaches a probe 20 with electrodes and filtering and concludes it would have been obvious to incorporate the teachings of Eggers with that of Acker and Rubinsky "to improve the efficacy of the medical procedure involving the characterization and treatment of tumors." Action, p. 5, (citing col. 3, lines 27-56 and col. 15, lines 33-53). Applicant respectfully

disagrees.

With respect to Claim 21, Applicant submits that one of skill in the art would not have combined the ablating or removing electrodes of Egger with the combination antenna and diagnostic sensing probe as claimed for brain therapy. First, there mere fact that distinct elements exist in separate prior art does not provide an enabling disclosure on how to achieve such a combination. Claim 21 claims a combination probe that provides three distinct functions on a small intra-brain probe, Eggers proposes just one. Claim 21 is restated below for ease of discussion.

21. An MRI combination imaging and interventional probe adapted to cooperate with an MRI scanner, the probe including a magnetic resonance imaging antenna configured to receive MR signals *in vivo* from local tissue when positioned inside the brain and a plurality of electrodes, at least one configured to detect local electrophysiological signals and at least one configured to apply stimulation or ablation energy to local tissue, the probe sized and configured for insertion into a brain of a patient during an *in vivo* MRI guided therapeutic treatment.

The Action states that Eggers teaches an MRI-compatible electrosurgical probe with electrodes for ablating intracranial tumors (citing to col. 3, lines 27-56) and the power source that supplies power to the electrode can have a filter (citing to col. 15, lines 33-53). The Action then concludes that it would have been obvious to incorporate the teachings of Eggers with that of Acker to improve the efficacy of the procedure involving the characterizations and treatment of tumors. Applicant respectfully disagrees.

As noted above, Eggers is a single-purpose probe. Claim 21 recites a multi-functional probe on a small intrabody probe. Claim 7 also recites that the probe has (at least) three different functions, Claim 16 recites the diagnostic function element and Claim 17 recites that the antenna and electrode are separate components of the probe.

With respect to the filters, Eggers states in a general way that the power source can have a filter for filtering leakage voltages less than 100 kHz. Eggers also states that alternatively, the power source can operate at 300-500 kHz where low frequency currents are a problem (col. 15, lines 44-65) and the use of inductors or LC components to control the

power input. Eggers proposes controlling the power source rather than attenuating any MRI scanner induced signal.

Further, and notably, Acker fails to describe either an MRI system or any MRI components. Rubinski proposes an MRI coil mounted on a cryoprobe and a coil mount with a second MRI coil mounted on it (bottom col. 16; & Claim 8). The brain emits no frequencies in the RF range. Eggers' invention is for delivering energy (RF: col. 28, line 7) for the purpose of treating aneurisms. Therefore Eggers cannot be used as a diagnostic electrode as recited in Claims 7-10, 16 and 21. Rubinski's device is a cryoprobe, which also cannot be used this way. The cited prior art, even combined, fail to teach or suggest the combination of elements claimed.

In summary, Eggers fails to teach or suggest a sensing electrode, nor a probe with MRI coils. Rubinsky proposes a cryoprobe, and Acker has no MRI capability. Thus, one of skill in the art would not have combined the references in the manner alleged by the Action in a manner that would yield the claimed invention.

Applicant also submits that the fact that different elements exist in different prior art references does not render the claimed combination obvious and that it is improper to combine selected features from discrete prior art references based only on the teachings of the present invention.

III. Related Pending Applications

Applicant respectfully notes that there are several co-pending continuations (and continuations-in-part) of parent application, U.S. 6,701,176 (for which the instant application includes a Terminal Disclaimer filed with the previous response) and the instant application, which the Applicant identifies below.

- 11/932,227 filed October 31, 2007, pending; (9450-14CT2);
- 11/924,877 filed October 26, 2007, pending; published 2003/0050557 March 13, 2003; (9450-19IP);
- 10/560,055 filed November 15, 2006, pending; published February 22, 2007 as US 2007-0042373; (9450-14CT);

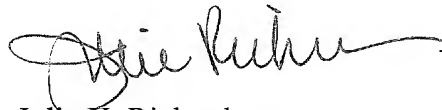
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- 10/123,534, filed November 15, 2006, pending; published April 29, 2007 as US Publication No. 2007-0088416; and
- 10/424,093, filed April 28, 2003, issued December 26, 2006 as US Patent No. 7,155,271.

CONCLUSION

Accordingly, Applicant submits that the present application is in condition for allowance and the same is earnestly solicited. Should the Examiner have any matters outstanding of resolution, he is encouraged to telephone the undersigned at 919-854-1400 for expeditious handling.

Respectfully submitted,



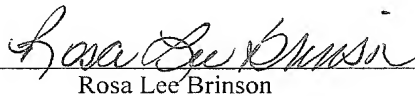
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